REMARKS

It is respectfully requested that the above supplemental amendments be entered pursuant to the provisions of 37 C.F.R. §1.116(b); that this application be reconsidered in view of the above amendments and the following remarks; and that all of the claims remaining in this application be allowed.

Amendments

Applicants make the following amendments to the claims of the present application assuming that the amendments requested in the January 5, 2004 Reply and Amendment pursuant to the provisions of 37 C.F.R. §1.116(b) have been entered.

Applicants have requested that Claim 1, 8, 10 and 12 be amended to correct an obvious typographical error, and specifically to indicate that Ar^1 through Ar^4 are independently either 1-alkylpyrrole or 1-cyclo***alkyalkyl***pyrrole wherein the pyrrole rings are attached to the amino group at the 4-position and the carbonyl group at the 1-position. The previous submission inadvertently described 1-cycloalkylpyrrole derivatives. Support for this amendment is found in Applicants' specification at, for example, page 27, lines 4-11 and on page 32 lines 1 – 15.

Applicants note that each of the above amendments has been requested solely to expedite allowance of what is believed to be allowable subject matter. Applicants reserve the right to file one or more continuation/divisional applications directed to the previously presented subject matter.

Applicants submit that each of the requested amendments either places the claims in condition for allowance or in a better condition for appeal. Accordingly, entry of these amendments pursuant to the provisions of 37 C.F.R. §1.116(b) is proper. Entry of these amendments is requested.

Upon entry of these amendments, Claims 1, 3-4, 6-14 and 20-21, are pending in this application. For the convenience of the Patent Office, a conformed copy of the pending claims is attached hereto which copy presumes that the requested amendments will be entered.

In view of the above, Applicants submit that this application is now in condition for allowance. A Notice to that effect is earnestly solicited.

CONCLUSION

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 50-2859** referencing docket no. 554912000200. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: January 14, 2004

Respectfully submitted,

By _____

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Palo Alto, California 94306
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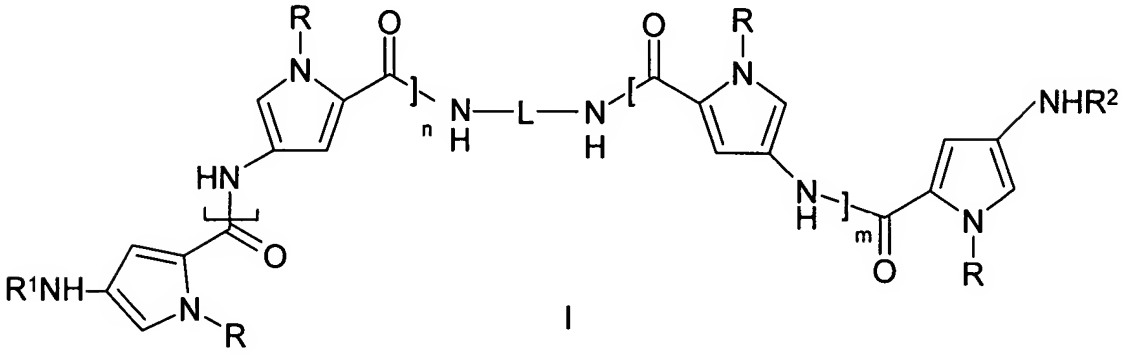
Attorney for Applicant

CONFORMED COPY OF THE PENDING CLAIMS

1. A compound of Formula (I):



I

wherein:

each R is independently alkyl or cycloalkylalkyl;

R^1 and R^2 are, independently of each other:

(i) hydrogen;

(ii) alkyl; or

(iii) $-COR^3$ wherein R^3 is selected from the group consisting of alkyl, amino, monosubstituted amino, disubstituted amino, or alkyl substituted with one, two or three substituents selected from the group consisting of amino, monosubstituted amino, disubstituted amino, guanidino, amidino, aminoacyl, $-NHCOR^a$ (wherein R^a is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, cycloalkyl, substituted cycloalkyl, cycloalkylalkyl, substituted cycloalkylalkyl, heteroaryl, substituted heteroaryl, heteroaralkyl, or substituted heteroaralkyl), $-NHCONHR^a$ (wherein R^a is as defined above), aryl, substituted aryl, heteroaryl, substituted heteroaryl, carboxy, alkoxycarbonyl, and $-OR^b$ (where R^b is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, cycloalkyl, substituted cycloalkyl, cycloalkylalkyl, substituted cycloalkylalkyl, heteroaryl, substituted heteroaryl, heteroaralkyl, or substituted heteroaralkyl), provided that at least one of R^1 and R^2 is a group that can form a pharmaceutically acceptable acid addition salt;

n and m are independently an integer from 0 to 4; and

L is:

(i) alkylene or cycloalkylene;

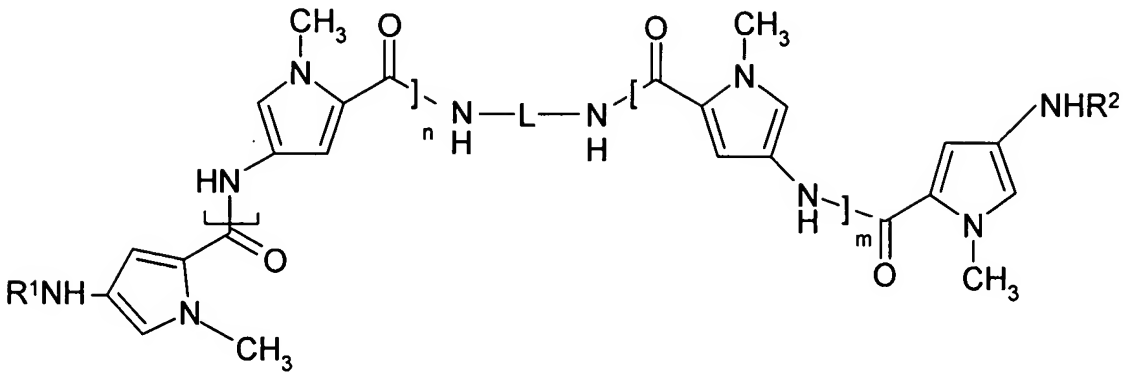
(ii) alkylene substituted with one, two or three substituent(s) selected from the group consisting of aryl, -CONHR^4 (wherein R^4 is hydrogen, alkyl, substituted alkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heteroaryl, substituted heteroaryl, heteroaralkyl, or substituted heteroaralkyl, heterocyclic, substituted heterocyclic, heterocyclicalkyl, heteroarylthioalkyl, or –(CHR^5)$_{n1}$-CO-(NH-Ar^3-CO)$_m$-NH-Ar^4-CO-NHR^3 where n1 is 1 to 3, R^5 is hydrogen or alkyl, substituted alkyl, and Ar^3, m, Ar^4, and R^3 are as defined above), -CONHNHR^6 [wherein R^6 is alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, -COR^7, -COOR^8 (wherein R^7 and R^8 are independently of each other alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, cycloalkyl, substituted cycloalkyl, cycloalkylalkyl, substituted cycloalkylalkyl, heteroaryl, substituted heteroaryl, or heteroaralkyl), heteroaryl, or heteroaralkyl], -NHR^9 (wherein R^9 is hydrogen, alkyl, substituted alkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, aminoalkylcarbonyl, or heterocycliccarbonyl), and guanidino; or

(iii) -(alkylene)$_x$-Z-(alkylene)$_y$-(Z^a)$_z$- wherein x, y and z are independently 0, 1, or 2 and Z and Z^a are, independently of each other, phenylene, cycloalkylene optionally fused to one or two phenylene ring(s), heterocyclene, -O-, -S-, -NR^{10}- [wherein R^{10} is hydrogen, alkyl, substituted alkyl, cycloalkylcarbonyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, -CONHR^4, -COR^7, -COOR^8 (where R^4, R^7 and R^8 are as defined above), -SO$_2$R^{11} (where R^{11} is alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heteroaryl, substituted heteroaryl, heteroaralkyl, or substituted heteroaralkyl) or -(CHR^5)$_{n2}$-NH-(CO-Ar^3-NH)$_m$-CO-Ar^4-NHR^2 where n2 is 2 to 4, R^5 is hydrogen, alkyl, or substituted alkyl, and Ar^3, m, Ar^4, and R^2 are as defined above], -CO-NH-, or -NH-CO-, provided that

when Z and/or Z^a is –NR^{10}- then it is separated from another nitrogen atom by at least two carbon atoms;

or a pharmaceutically acceptable salt thereof.

3. A compound of the formula:



R^1 and R^2 are, independently of each other:

(i) hydrogen;

(ii) alkyl; or

(iii) $-COR^3$ wherein R^3 is selected from the group consisting of alkyl, amino, monosubstituted amino, disubstituted amino, or alkyl substituted with one, two or three substituents selected from the group consisting of amino, monosubstituted amino, disubstituted amino, guanidino, amidino, aminoacyl, $-NHCOR^a$ (wherein R^a is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, cycloalkyl, substituted cycloalkyl, cycloalkylalkyl, substituted cycloalkylalkyl, heteroaryl, substituted heteroaryl, heteroaralkyl, or substituted heteroaralkyl), $-NHCONHR^a$ (wherein R^a is as defined above), aryl, substituted aryl, heteroaryl, substituted heteroaryl, carboxy, alkoxycarbonyl, and $-OR^b$ (where R^b is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, cycloalkyl, substituted cycloalkyl, cycloalkylalkyl, substituted cycloalkylalkyl, heteroaryl, substituted heteroaryl, heteroaralkyl, or substituted heteroaralkyl), provided that at least one of R^1 and R^2 is a group that can form a pharmaceutically acceptable acid addition salt;

n and m are independently an integer from 0 to 4; and

L is:

(i) alkylene or cycloalkylene;

(ii) alkylene substituted with one, two or three substituent(s) selected from the group consisting of aryl, $-CONHR^4$ (wherein R^4 is hydrogen, alkyl, substituted alkyl, hydroxyalkyl,

alkoxyalkyl, aminoalkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heteroaryl, substituted heteroaryl, heteroaralkyl, or substituted heteroaralkyl, heterocyclic, substituted heterocyclic, heterocyclicalkyl, heteroarylthioalkyl, or $-(CHR^5)_{n1}$-CO-$(NH-Ar^3-CO)_m$-NH-Ar^4-CO-NHR^3 where n1 is 1 to 3, R^5 is hydrogen or alkyl, substituted alkyl, and Ar^3, m, Ar^4, and R^3 are as defined above), -$CONHNHR^6$ [wherein R^6 is alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, -COR^7, -$COOR^8$ (wherein R^7 and R^8 are independently of each other alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, cycloalkyl, substituted cycloalkyl, cycloalkylalkyl, substituted cycloalkylalkyl, heteroaryl, substituted heteroaryl, or heteroaralkyl), heteroaryl, or heteroaralkyl], -NHR^9 (wherein R^9 is hydrogen, alkyl, substituted alkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, aminoalkylcarbonyl, or heterocycliccarbonyl), and guanidino; or

(iii) $-(alkylene)_x$-Z-$(alkylene)_y$-$(Z^a)_z$- wherein x, y and z are independently 0, 1, or 2 and Z and Z^a are, independently of each other, phenylene, cycloalkylene optionally fused to one or two phenylene ring(s), heterocyclene, -O-, -S-, -NR^{10}- [wherein R^{10} is hydrogen, alkyl, substituted alkyl, cycloalkylcarbonyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, -$CONHR^4$, -COR^7, -$COOR^8$ (where R^4, R^7 and R^8 are as defined above), -SO_2R^{11} (where R^{11} is alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heteroaryl, substituted heteroaryl, heteroaralkyl, or substituted heteroaralkyl) or $-(CHR^5)_{n2}$-NH-$(CO-Ar^3-NH)_m$-CO-Ar^4-NHR^2 where n2 is 2 to 4, R^5 is hydrogen, alkyl, or substituted alkyl, and Ar^3, m, Ar^4, and R^2 are as defined above], -CO-NH-, or -NH-CO-, provided that

when Z and/or Z^a is $-NR^{10}$- then it is separated from another nitrogen atom by at least two carbon atoms;

or a pharmaceutically acceptable salt thereof.

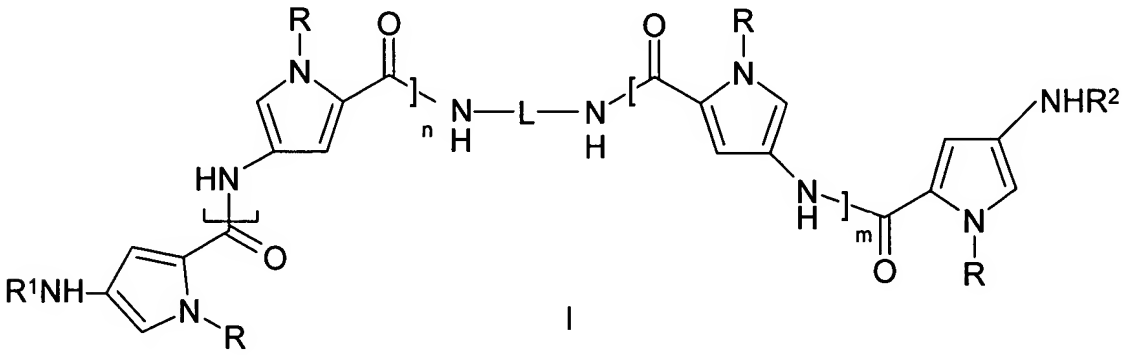
4. The compound of Claim 1 wherein n and m are 0 or 1.

6. The compound of Claim 1 wherein R^1 and R^2 are independently -COR^3.

7. The compound of Claim 6 wherein R^1 and R^2 are independently aminomethylcarbonyl, 1-amino-4-guanidinobutylcarbonyl, 1,4-diaminobutylcarbonyl, 1,5-

diaminopentyl-carbonyl, 1-amino-5-(3,4difluorophenylureido)pentylcarbonyl, 1-(3,4-difluoro-phenylureido)-4-guanidinobutylcarbonyl, 1-[4-(N,N-(2-chloroethyl)-aminophenylbutanoyl)]amino-4-guanidinobutylcarbonyl, or 1-amino-5-[4-(N,N-(2-chloroethyl)-aminophenyl-butanoyl)]aminopentylcarbonyl.

8. A compound of the Formula (I):



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wherein:

each R is independently alkyl or cycloalkylalkyl;

R^1 and R^2 are, independently of each other:

(i) hydrogen;

(ii) alkyl; or

(iii) $-COR^3$ wherein R^3 is selected from the group consisting of alkyl, amino, monosubstituted amino, disubstituted amino, or alkyl substituted with one, two or three substituents selected from the group consisting of amino, monosubstituted amino, disubstituted amino, guanidino, amidino, aminoacyl, $-NHCOR^a$ (wherein R^a is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, cycloalkyl, substituted cycloalkyl, cycloalkylalkyl, substituted cycloalkylalkyl, heteroaryl, substituted heteroaryl, heteroaralkyl, or substituted heteroaralkyl), $-NHCONHR^a$ (wherein R^a is as defined above), aryl, substituted aryl, heteroaryl, substituted heteroaryl, carboxy, alkoxycarbonyl, and $-OR^b$ (where R^b is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, cycloalkyl, substituted cycloalkyl,

cycloalkylalkyl, substituted cycloalkylalkyl, heteroaryl, substituted heteroaryl, heteroaralkyl, or substituted heteroaralkyl), provided that at least one of R^1 and R^2 is a group that can form a pharmaceutically acceptable acid addition salt;

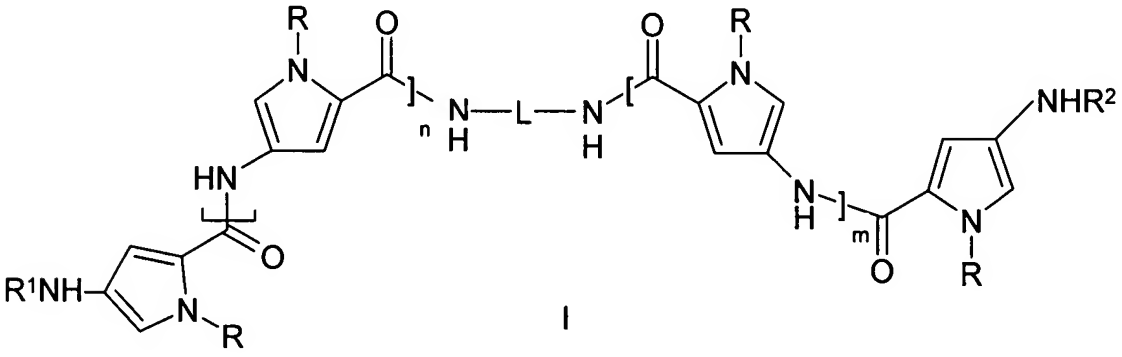
n and m are independently an integer from 0 to 4; and

L is alkylene;

or a pharmaceutically acceptable salt thereof.

9. The compound of Claim 8 wherein L is 1,2-ethylene, 1,3-propylene, 1,4-butylene, 1,6-hexylene, 1,8-octylene, 1,12-dodecylene, 1-methylethylene, or 1,2-hexadecylene.

10. A compound of the Formula (I):



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wherein:

each R is independently alkyl or cycloalkylalkyl;

R^1 and R^2 are, independently of each other:

(i) hydrogen;

(ii) alkyl; or

(iii) $-COR^3$ wherein R^3 is selected from the group consisting of alkyl, amino, monosubstituted amino, disubstituted amino, or alkyl substituted with one, two or three substituents selected from the group consisting of amino, monosubstituted amino, disubstituted amino, guanidino, amidino, aminoacyl, $-NHCOR^a$ (wherein R^a is hydrogen, alkyl, substituted alkyl, aryl,

substituted aryl, aralkyl, substituted aralkyl, cycloalkyl, substituted cycloalkyl, cycloalkylalkyl, substituted cycloalkylalkyl, heteroaryl, substituted heteroaryl, heteroaralkyl, or substituted heteroaralkyl), -NHCONHR^a (wherein R^a is as defined above), aryl, substituted aryl, heteroaryl, substituted heteroaryl, carboxy, alkoxycarbonyl, and -OR^b (where R^b is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, cycloalkyl, substituted cycloalkyl, cycloalkylalkyl, substituted cycloalkylalkyl, heteroaryl, substituted heteroaryl, heteroaralkyl, or substituted heteroaralkyl), provided that at least one of R^1 and R^2 is a group that can form a pharmaceutically acceptable acid addition salt;

n and m are independently an integer from 0 to 4; and

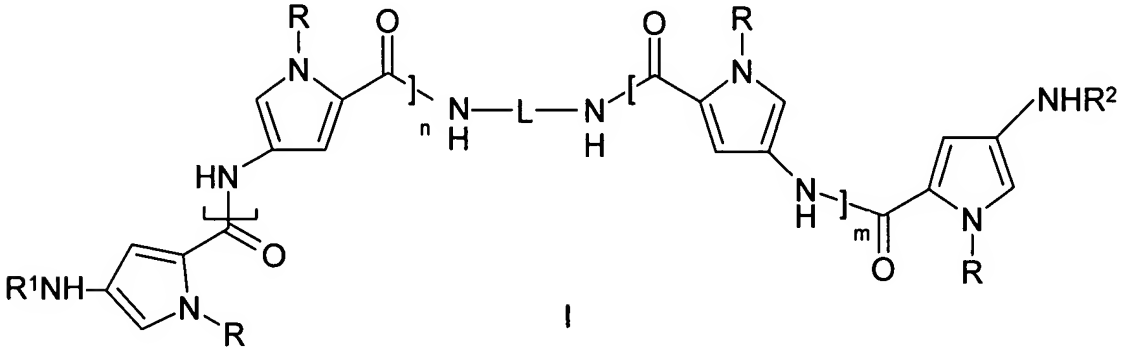
L is alkylene substituted with one, two or three substituent(s) selected from the group consisting of aryl, -CONHR^4 (wherein R^4 is hydrogen, alkyl, substituted alkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heteroaryl, substituted heteroaryl, heteroaralkyl, or substituted heteroaralkyl, heterocyclic, substituted heterocyclic, heterocyclicalkyl, heteroarylthioalkyl, or –(CHR^5)$_{n1}$-CO-(NH-Ar^3-CO)$_m$-NH-Ar^4-CO-NHR^3 where n1 is 1 to 3, R^5 is hydrogen or alkyl, substituted alkyl, and Ar^3, m, Ar^4, and R^3 are as defined above), -CONHNHR^6 [wherein R^6 is alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, -COR^7, -COOR^8 (wherein R^7 and R^8 are independently of each other alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, cycloalkyl, substituted cycloalkyl, cycloalkylalkyl, substituted cycloalkylalkyl, heteroaryl, substituted heteroaryl, or heteroaralkyl), heteroaryl, or heteroaralkyl], -NHR^9 (wherein R^9 is hydrogen, alkyl, substituted alkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, aminoalkylcarbonyl, or heterocycliccarbonyl), and guanidino;

or a pharmaceutically acceptable salt thereof.

11. The compound of Claim 10 wherein L is meso-1,2-diphenylethylene, 1-(p-nitrophenylaminocarbonyl)-1,5-pentylene, 1-(napth-2-ylaminocarbonyl)-1,5pentylene, 1-(pentafluorophenylhydrazidocarbonyl)-1,5-pentylene, 1-(5-trifluoro-pyrimidin-2-ylhydrazidocarbonyl)-1,5-pentylene, 1-(2-pyrene-lylethylamino-carbonyl)-1,5-pentylene, 1-[2-(6-nitrobenzimidazol-1-ylethylaminocarbonyl]-1,5-pentylene, 1-[2-(indol-3-yl)-ethylaminocarbonyl]-1,5-pentylene, 1-[2-(5-fluoroindol-3-yl)ethylaminocarbonyl]-1,5-pentylene, 1-[2-(4-nitrophenyl)ethylaminocarbonyl]-1,5-pentylene, 1-(benzyloxycarbonyl-hydrazidocarbonyl)-1,2-

ethylene, 1-(napth-l-ylaminocarbonyl)-1,5-pentylene, 1-(4-pyrene-1-ylbutylaminocarbonyl)-1,5-pentylene, l-(2-(2-trifluoromethylquinolin-4-yl)thio-ethylaminocarbonyl)-1,5-pentylene, 1-(pentafluorophenylhydrazidocarbonyl)-1,4-butylene, 1-(4-pyrene-1-ylmethylaminocarbonyl)-1,5-pentylene, 1-(2-hydroxyethylaminocarbonyl)-1,5-pentylene, 1-(2-aminoethylaminocarbonyl)-1,5-pentylene, 1-(3-dimethylaminopropyl-aminocarbonyl)-1,5-pentylene, 1-(bis-(2-aminoethyl)aminoethylaminocarbonyl)-1,5-pentylene, 1-(N-(2-aminoethyl)aminoethylaminocarbonyl)-1,5-pentylene, 2-(aminomethylcarbonyl-amino)-1,3-propylene, or 2-(3-hydroxypyrrolidin-5-ylcarbonyl-amino)-1,3-propylene.

12. A compound of the Formula (I):



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wherein:

each R is independently alkyl or cycloalkylalkyl;

R^1 and R^2 are, independently of each other:

(i) hydrogen;

(ii) alkyl; or

(iii) $-COR^3$ wherein R^3 is selected from the group consisting of alkyl, amino, monosubstituted amino, disubstituted amino, or alkyl substituted with one, two or three substituents selected from the group consisting of amino, monosubstituted amino, disubstituted amino, guanidino, amidino, aminoacyl, $-NHCOR^a$ (wherein R^a is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, cycloalkyl, substituted cycloalkyl, cycloalkylalkyl,

substituted cycloalkylalkyl, heteroaryl, substituted heteroaryl, heteroaralkyl, or substituted heteroaralkyl), -NHCONHR^a (wherein R^a is as defined above), aryl, substituted aryl, heteroaryl, substituted heteroaryl, carboxy, alkoxycarbonyl, and -OR^b (where R^b is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, cycloalkyl, substituted cycloalkyl, cycloalkylalkyl, substituted cycloalkylalkyl, heteroaryl, substituted heteroaryl, heteroaralkyl, or substituted heteroaralkyl), provided that at least one of R^1 and R^2 is a group that can form a pharmaceutically acceptable acid addition salt;

n and m are independently an integer from 0 to 4; and

L is -(alkylene)$_x$-Z-(alkylene)$_y$-(Z^a)$_z$- wherein x, y and z are independently 0, 1, or 2 and Z and Z^a are, independently of each other, phenylene, cycloalkylene optionally fused to one or two phenylene ring(s), heterocyclene, -O-, -S-, -NR^{10}- [wherein R^{10} is hydrogen, alkyl, substituted alkyl, cycloalkylcarbonyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, -CONHR^4, -COR^7, -COOR^8 (where R^4, R^7 and R^8 are as defined above), -SO$_2$R^{11} (where R^{11} is alkyl, substituted alkyl, aryl, substituted aryl, aralkyl, substituted aralkyl, heteroaryl, substituted heteroaryl, heteroaralkyl, or substituted heteroaralkyl) or -(CHR^5)$_{n2}$-NH-(CO-Ar^3-NH)$_m$-CO-Ar^4-NHR^2 where n2 is 2 to 4, R^5 is hydrogen, alkyl, or substituted alkyl, and Ar^3, m, Ar^4, and R^2 are as defined above], -CO-NH-, or -NH-CO-,

provided that when Z and/or Z^a is –NR^{10}- then it is separated from another nitrogen atom by at least two carbon atoms;

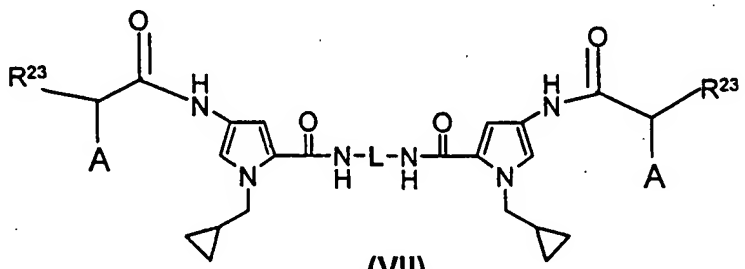
or a pharmaceutically acceptable salt thereof.

13. The compound of Claim 12 wherein L is m-xylene, p-xylene, 2,7-fluorendiyl, *bis*-(3-N-benzyloxycarbonylamino)propylene [-(CH$_2$)$_3$-N(BzOCO-)-(CH$_2$)$_3$-], *bis*-(2-napth-2-ylsulfonylamino)ethylene [-(CH$_2$)$_2$-N(-SO$_2$napth-2-yl)-(CH$_2$)$_2$-], *bis*-(2-N-3,5-dinitrophenylcarbonylamino)ethylene [-(CH$_2$)$_2$-N(-CO-3,5-dinitrophenyl)-(CH$_2$)$_2$-], 1,3-cyclohexyl-bis-methylene [-(CH$_2$)-(1,3-C$_6$H$_{10}$)-(CH$_2$)-], 1,4-cyclohexyl-bis-methylene [-(CH$_2$)-(1,4-C$_6$H$_{10}$)-(CH$_2$)-], 4,4'-methylene-bis-1,4-cyclohexylene [-(1,4-C$_6$H$_{10}$)-(CH$_2$)-(1,4-C$_6$H$_{10}$)-], 1,2-cyclohexylene (1,2-C$_6$H$_{10}$-), *bis*-(2-adamantyll-ylcarbonylamino)ethylene, *bis*-(3-N-methylamino)propylene [-(CH$_2$)$_3$-N(-CH$_3$)-(CH$_2$)$_3$-], *bis*-(3-amino)propylene [-(CH$_2$)$_3$-NH-(CH$_2$)$_3$-], 1,4-piperazino- *bis*-propylene [-(CH$_2$)$_3$-(1,4-piperazino)-(CH$_2$)$_3$-] , *bis*-(2-(2-

aminoethyl)amino)ethylene [-$(CH_2)_2$-N(-$(CH_2)_2NH_2$)-$(CH_2)_2$-], and *bis*-(2-amino)ethylene [-$(CH_2)_2$-NH-$(CH_2)_2$-] .

14. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claims 1, 3-4 and 6-13 and a pharmaceutically suitable carrier.

20. A compound of claim 1 which compound is represented by formula (VII)



(VII)

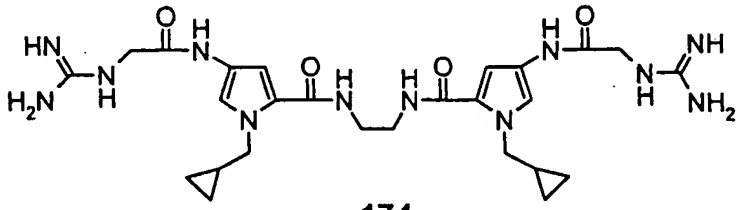
wherein

L is selected from the group consisting of alkylene and cycloalkylene;

A is an amino acid side chain; and

R^{23} is selected from the group consisting of guanidino, amino, and ornithylamino.

21. A compound of claim 20 selected from the group consisting of



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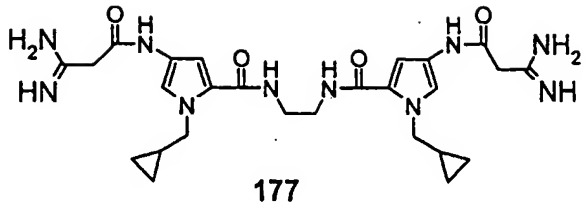

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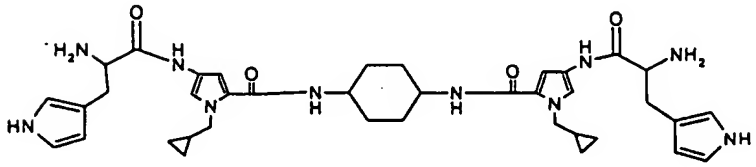

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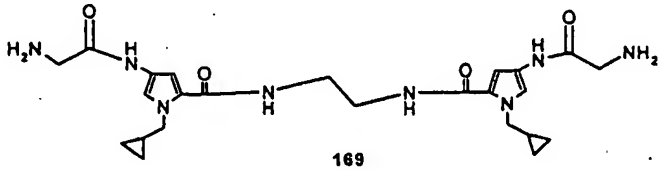

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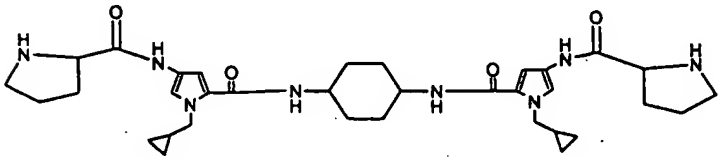

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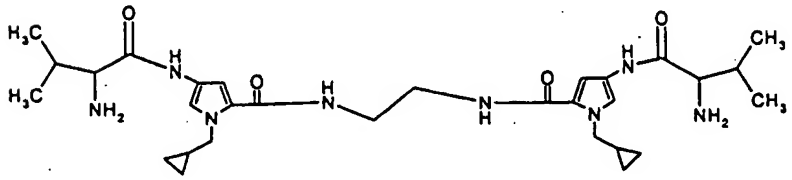

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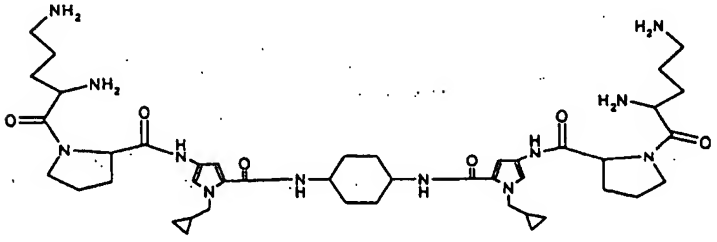

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and pharmaceutically acceptable salts thereof.